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08/884,873	06/30/1997	PHILLIP DAN COOK	ISIS-2202	6678

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EXAMINER

BAKER, MAURIE GARCIA

ART UNIT

PAPER NUMBER

1627

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28

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No. <b>08/884,873</b>	Applicant(s) <b>Cook</b>
Examiner <b>Maurie Garcia Baker, Ph. D.</b>	Art Unit <b>1627</b>

*-- The MAILING DATE of this communication appars on the cover sheet with the correspondence address --*

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE THREE MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

1)  Responsive to communication(s) filed on Apr 26, 2002

2a)  This action is **FINAL**. 2b)  This action is non-final.

3)  Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle* 35 C.D. 11; 453 O.G. 213.

### Disposition of Claims

4)  Claim(s) 2-5, 7-12, and 33 is/are pending in the application.

4a) Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

5)  Claim(s) \_\_\_\_\_ is/are allowed.

6)  Claim(s) 2-5, 7-12, and 33 is/are rejected.

7)  Claim(s) \_\_\_\_\_ is/are objected to.

8)  Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

9)  The specification is objected to by the Examiner.

10)  The drawing(s) filed on \_\_\_\_\_ is/are a)  accepted or b)  objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)  The proposed drawing correction filed on \_\_\_\_\_ is: a)  approved b)  disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)  The oath or declaration is objected to by the Examiner.

### Priority under 35 U.S.C. §§ 119 and 120

13)  Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)  All b)  Some\* c)  None of:

1.  Certified copies of the priority documents have been received.

2.  Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.

3.  Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\*See the attached detailed Office action for a list of the certified copies not received.

14)  Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a)  The translation of the foreign language provisional application has been received.

15)  Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

### Attachment(s)

1) <input type="checkbox"/> Notice of References Cited (PTO-892)	4) <input checked="" type="checkbox"/> Interview Summary (PTO-413) Paper No(s). <u>26</u>
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)
3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____	6) <input type="checkbox"/> Other: _____

## DETAILED ACTION

### ***Request for Continued Examination***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's previously unentered submission filed on July 23, 2001 has been entered.
  
2. In the submission filed July 23, 2001, claim 33 was amended and no claims were cancelled or added. Therefore, claims 2-5, 7-12 and 33 are pending and under examination.
  
3. Please note the following (from Paper No. 20; emphasis added):

The examiner would like to point out that a search of applicants *specific* elected species did not result in identification of any prior art. Thus, the search was extended as per MPEP § 803.02 “should no prior art be found that anticipates or renders obvious the elected species, the search of the Markush-type claim will be extended. If prior art is then found that anticipates or renders obvious the Markush-type claim with respect to a nonelected species, the Markush-type claim shall be rejected and claims to the nonelected species held withdrawn from further consideration. **The prior art search, however, will not be extended unnecessarily to cover all nonelected species**”. The examiner has extended the search to include all compounds containing the pyrimidine scaffold structure as set forth in claim 33 (compound I).

***Withdrawn Rejections***

4. The previous rejection under 35 USC 112, first paragraph (new matter) is withdrawn in view of applicant's arguments (in the Brief filed February 13, 2002).

***Claim Rejections - 35 USC § 112***

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 33 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear what is the specific structure of the compounds of formula I because the L moiety is *incompletely defined*. For example, if L is a moiety such as “keto”, “carboxyl” or “amidine”, what is the actual structure of such a group? That is, denoting the group as “keto” (for example) does not fully define what ketone is being referred to. The same is true for many of the moieties listed for the instant L group. This adds considerable confusion to the claim.

***Claim Rejections - 35 USC § 103***

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject

matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. Claims 2-5, 7-12 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gordeev et al (WO 96/33972), Grandoni (US 5,998,420) and Hamprecht et al (US 5,591,694) in view of Gordon et al (of record, J. Med. Chem. 1994, Vol. 37, No. 10, pp. 1385-1401).

Gordeev et al teach methods for synthesizing libraries of pyrimidine compounds (see Abstract). The library compounds of Gordeev et al have the claimed heterocyclic scaffold and substitution pattern (see page 34-35 and more specifically page 81) and are substantially homogeneous (page 35, bottom). The library compounds are made in a pooled format (see page 84, lines 18-28), for example, a pool of 21 pyrimidines is made and tested. This reads directly on the limitation of a mixture of at least 6 compounds and the further limitations of claims 2 and 3. All compounds are present in at least some of the pools and the compounds are synthesized at a purity (see page 81) where the mixture would be close to equimolarity. The pyrimidine compounds of Gordeev et al have at least three functionalizable atoms, at least one of which is nitrogen (see pages 81-85). In the compounds of Gordeev et al the tethers can be considered to be bonds for two of the side groups and the amine moiety could be considered a tether moiety (NHR<sup>1</sup>). This meets the limitations of claims 5 and 7-10. The building blocks of the library comprise various leaving groups (see page 83), reading on the limitations of claims 11 and 12.

Gordeev et al lacks the specific teaching of the instantly claimed compounds of the library (specific T and L combinations).

However, Grandoni et al teach sulfonylurea herbicides that read on the claimed compounds (see Figures 3 & 5, for example). The pyrimidine compounds have least three functionalizable atoms, at least one of which is nitrogen, oxygen and/or sulfur and have groups that can be considered tethers (see structures **S**, **T**, **U** and **V** in Figure 5 and compound at the bottom of Figure 6). The building blocks of the library comprise various leaving groups (see column 9, top). In the context of creating better inhibitors of acetolactate synthase (beginning in column 8 and going through the top of column 10), Grandoni et al teach the concept of "combinatorial optimization of inhibitory sulfonylureas" (column 9).

Hamprecht et al also teach sulfonylurea herbicides (see Abstract). These compounds also read on those in the claimed mixture and have similar substitution to those of Grandoni. Hamprecht et al teach that compounds with improved properties are needed and that to do so, varying the substituents on the pyrimidine moiety is a preferred method of doing so (see column 2, lines 12-23).

Grandoni and Hamprecht et al lack the teaching of creating a mixture of at least 6 compounds.

However, Gordeev et al teach these limitations, see above. Also, Gordon et al teaches that "[w]hen small molecule leads for a target have been previously defined...the notion of searching for more potent derivatives among libraries combinatorially enriched in specific pharmacophore analogs is an obvious tactic

to pursue" (p.1386 Column 1, 1<sup>st</sup> full paragraph). Also, Gordon et al teaches the general principles of combinatorial chemistry and the rationale for creating libraries, see page 1385 and 1397-1401 generally. Specifically, the notion of intentional biasing as a form of drug design is taught (see page 1401, 1<sup>st</sup> column). Gordon et al teaches a "spectrum of molecular diversity" (see page 1397, Figure 19) that describes why a library of a certain size would be useful for a variety of different applications.

Therefore, it would have been *prima facie* obvious to one of ordinary skill to create a mixture (i.e. library) of six or more compounds of the claimed type based on the teachings Grandoni and Hamprechet et al as to the synthesis and uses of such compounds and the teachings of Gordeev et al and Gordon et al regarding libraries. A person of ordinary skill in the art would have been motivated to create libraries to have large numbers of molecules available for testing for improved properties (see Gordon, page 1398, 1<sup>st</sup> paragraph).

***Response to Arguments***

9. Applicant's arguments filed July 23, 2001 have been fully considered but are moot in view of the new grounds of rejection set forth in this action.

***Status of Claims/Conclusion***

10. No claims are allowed

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maurie Garcia Baker, Ph.D. whose telephone number is (703) 308-0065. The examiner can normally be reached on Monday-Thursday and alternate Fridays from 9:30 to 7:00.

12. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jyothsna Venkat, can be reached on (703) 308-2439. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Maurie Garcia Baker, Ph.D.  
June 30, 2002



MAURIE E. BAKER  
PATENT EXAMINER